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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,500	11/21/2003	Joseph Chappell	50229-419	8924

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,500	CHAPPELL ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/10/2006.

Applicant's election with traverse of Group II claims 10-14 in the reply filed on 8/10/2006 is acknowledged. The traversal is on the ground(s) that the Groups are drawn to related subject material and can be searched together without any additional or serious burden upon the office. This is not found persuasive because the two groups are sufficiently divergent in their scope to permit restriction into two separate groups. The search and examination for the polypeptide would not encompass the search and examination of vectors, transformed cells and plants.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9 are withdrawn. Claims 16-19 are newly added and will be examined with the elected group. Claims 10-19 are examined

Drawings

CH 3 in Figure 6 shows the second active domain as having diagonal stripes when vertical stripes have been used to describe the active domain in the other sections of the figure.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims DNA encoding a chimeric isoprenoid synthase polypeptide of unspecified activity that comprises a first isoprenoid synthase polypeptide of unspecified activity joined to a second and different isoprenoid synthase polypeptide of unspecified activity; and vectors and transformed cells and plants thereof.

Applicant describes TEAS and HVS cDNA incorporated through reference (Back and Chappell, J. Biol. Chem. 1995, Vol. 270, pp. 7375); oligonucleotides of SEQ ID NO: 1-6 for constructing chimeric synthases; domain maps of chimeric sesquiterpene synthases CH1-CH14 in Figure 4a comprising sections of TEAS and HVS; Figure 6 shows the domain switching strategy that produced CH4 and resulted in a synthase having an altered enzyme activity with respect to the ratio of products; Figures 7 and 8 show hypothetical domain switching and hypothetical reaction products for chimeric quiescent-casbene synthase and chimeric quiescent-cadinene synthase. Applicant has only described chimeric isoprenoid synthases CH4 and CH10-CH14 that synthesized 5-epi-aristolochene and vetispiradene in varying ratios when transformed

into E. coli on page 17 in Table 1, wherein 5-epi-aristolochene and vetispiradene are the natural products of the respective wild type tobacoo and hanbane enzymes domains of which are comprised within the chimera.

Applicant does not describe chimeric isoprenoid synthases that are comprised of a first isoprenoid synthase and a second and different isoprenoid synthase in their entirety or in portions thereof, other than the domain maps of chimeric sesquiterpene synthases CH1-CH14.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of chimeric isoprenoid synthases comprising a first isoprenoid synthase joined to a second and different isoprenoid synthase. Applicants only describe chimeric variants CH4 and CH10-CH14 comprising portions of sesquiterpene synthases TEAS and HVS. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of chimeric isoprenoid synthases. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for chimeric isoprenoid synthases of non-specified activity, it remains unclear what features identify a chimeric isoprenoid synthase that comprise a first and second and different isoprenoid synthase. Since the

genus of chimeric isoprenoid synthases has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Based upon the disclosure of TEAS and HVS, there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of the broadly claimed chimeric isoprenoid synthases, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences, the disclosure of TEAS and HVS chimeric variants CH4 and CH10-CH14, does not provide adequate description of the broadly claimed genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of chimeric isoprenoid synthases, other than chimeric variants of comprising TEAS and HVS, CH4 and CH10-CH14, as broadly claimed.

Claims 10-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims DNA encoding a chimeric isoprenoid synthase polypeptide that comprises a first isoprenoid synthase polypeptide joined to a second and different isoprenoid synthase polypeptide; and vectors and transformed cells and plants thereof.

Applicant teaches TEAS and HVS cDNA incorporated through reference (Back and Chappell, J. Biol. Chem. 1995, Vol. 270, pp. 7375); oligonucleotides of SEQ ID NO: 1-6 for constructing chimeric synthases; domain maps of chimeric sesquiterpene synthases CH1-CH14 in Figure 4a comprising sections of TEAS and HVS; Figure 6 shows the domain switching strategy that produced CH4 and resulted in a synthase having an altered enzyme activity; Figures 7 and 8 show hypothetical domain switching and hypothetical reaction products for chimeric quiescent-casbene synthase and chimeric quiescent-cadinene synthase; cloning of CH1-CH14 using said oligonucleotides of SEQ ID NO: 1-6 on pages 10-16; altered aristolochene and vetispiradene ratios produced by CH4 and CH10-CH14 when transformed into E. coli on page 17 in Table 1; and the structure for potential chimeric quiescent synthases on pages 18-19; and potential chimeric casbene and cadiene synthases on pages 19-20; and prophetic transformation and expression of bacteria, yeast and plants using said chimeric synthases on pages 20-36.

Applicant does not teach an isolated DNA encoding a chimeric isoprenoid synthase comprising a first and a second isoprenoid synthase that are different from each other than CH4 and CH10-CH14.

Designing chimeric proteins that for example have modified catalytic function and altered products is highly unpredictable especially when changes are extrapolated onto similar

enzymes that do not share the same biochemical mechanism. Without appropriate guidance, one of skill in the art would not know which domains or which isoprenoid synthases when swapped or combined would be effective. The unpredictability is evident in a newly defined group of monoterpene synthases, a sub group of the claimed isoprenoid synthases, isolated from snapdragon (Dudareva N. et al., The Plant Cell, May 2003, Vol. 15, p. 1227-1241; see page 1237 column 2 and page 1238 Figure 10). The isolated polynucleotides did not encode a conserved protein motif that is associated with the biochemical mechanism of the monoterpene synthases identified previously from other plant species and were lacking a 200 amino acid region common to the subfamily. Hence there appears to be a different mechanism at work in the monoterpene synthases isolated from snapdragon as compared to other species. Therefore, not all isoprenoid synthases are similar enough to allow for general assumptions in their redesign or recombination into chimeric structures.

Given the unpredictability in the art as to which domains from which plants would tolerate chimerization; the breadth of the claims encompassing any plant cell comprising any number of enzymatic domains or full length enzymatic sequences selected from a broad category of isoprenoid synthases; the lack of guidance in the specification or in the prior art as to which isoprenoid synthases or domains of the isoprenoid synthase enzyme super-family would best serve the invention; one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictably eliminated. Thus, undue trail and error experimentation would be needed to make and clone a multitude of non-exemplified isoprenoid synthase chimeras and to test them in a myriad of non-exemplified expression systems for a multitude of

non-exemplified isoprenoid products. Therefore, the invention is not enabled for the scope set forth in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Visser R. *et al.* Plant Molecular Biology, 1991: Vol 17; pp. 691-699.

The claim is broadly drawn to a vector comprising a chimeric synthase gene and a dominant selectable marker.

Visser teaches a transformation construct comprising a chimeric synthase and a dominant selectable marker (See Abstract lines 1-10; where the GUS gene is the dominant selectable marker and the chimeric granule bound starch synthase-GUS gene comprises a promoter regulatory region because it is expressed in a transformed plant and is a chimeric synthase gene; see title); and thus the reference teaches all the limitations of Claims 16-17.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-21 and 25-27 of copending Application No. 09/514,513. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chimeric isoprenoid synthases and transformed plants of the instant Application are obvious over the chimeric isoprenoid synthases having assemetrically placed domains and transformed plants of U.S. 09/514,513.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

All claims are rejected.

Claims 10-15 and 18-19 are deemed free of the prior art given the failure of the prior art to teach or suggest a cimeric isoprenoid synthase joined to a seconed and different isoprenoid synthase.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
November 27, 2006

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER

Russell Kallis